WHAT IS CLAIMED IS:

1. A compound of Formula I

5 I

or a pharmaceutically acceptable salt thereof, wherein

R¹ is selected from the group consisting of:

- 10 (a) S(O)₂CH₃,
 - (b) $S(O)_2NH_2$,
 - (c) S(O)₂NHC(O)CF₃,
 - (d) $S(O)(NH)CH_3$,
 - (e) $S(O)(NH)NH_2$,
- 15 (f) $S(O)(NH)NHC(O)CF_3$,
 - (g) P(O)(CH3)OH, and
 - (h) P(O)(CH₃)NH₂;

 ${\rm R}^2$ and ${\rm R}^3$ each are independently selected from the group consisting of:

- (a) hydrogen,
- 20 (b) halo,
 - (c) C₁₋₆alkoxy,
 - (d) C₁₋₆alkylthio,
 - (e) CN,
 - (f) CF₃,
- 25 (g) C₁₋₆alkyl, and
 - (h) N3;

R4 is selected from the group consisting of

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- (a) hydrogen,
- (b) C₁₋₆alkyl, optionally substituted with 1-3 substituents independently selected from the group consisting of:
 - (i) halo,

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(ii) phenyl, naphthyl or HET¹, each of said phenyl, naphthyl or HET¹ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁶,

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- (iii) N(Rⁱ)Rⁱⁱ, wherein Rⁱ and Rⁱⁱ are each independently selected from the group consisting of hydrogen and C₁₋₄alkyl,
- (iv) -CO2Riii, wherein Riii is hydrogen or C1-4alkyl,
- (c) phenyl, naphthyl or HET², each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁶;

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R⁵ is selected from the group consisting of:

- (a) $-NO_S$,
- (b) $-C(O)-E-C_{1-10}$ alkyl-W-NO_S,
- (c)

 $\begin{array}{c} O & (R^a)_{0-3} \\ --C-E-C_{0-6}alkyl--Ar-C_{0-6}alkyl--W--NO_s \end{array}$

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wherein:

each s is independently 1 or 2,

E is a bond, oxygen, sulfur or -C(O)-O-,

each W is independently selected from the group consisting of:

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- (1) oxygen,
- (2) sulfur,
- (3)

$$CO_2R^b$$
 $-C$
 CO_2R^b

(4)

$$\begin{array}{ccc} O & CO_2R^b \\ --C-C-- & \\ R^b \end{array}$$

Ar is selected from the group consisting of: phenyl, naphthyl and HET3,

each Ra is independently selected from the group consisting of:

- 5 (1) halo,
 - (2) C₁₋₆alkyl,
 - (3) C₁₋₆alkoxy,
 - (4) C₁₋₆alkylthio,
 - (5) OH,
 - (6) CN,

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- (7) CF₃,
- (8) CO_2R^7 , and
- (9) C₀₋₆alkyl-W-NO_s;

each Rb is independently selected from the group consisting of:

- (1) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET⁴, each of said phenyl, naphthyl or HET⁴ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁸; and
- (2) phenyl, naphthyl or HET⁵, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁸;

 R^6 , R^7 and R^8 are each independently selected from the group consisting of

- (a) hydrogen,
- (b) C₁₋₆alkyl; and
- HET¹, HET², HET³, HET⁴ and HET⁵ are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl,

indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydrothiadiazolyl, dihydrothiazolyl, tetrahydrofuranyl, and tetrahydrothienyl.

2. A compound according to Claim 1 of Formula I

 R^1 $O-R^5$ R^2 O R^4 I

or a pharmaceutically acceptable salt thereof, wherein

R1 is selected from the group consisting of:

(a) $S(O)_2CH_3$,

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- (b) $S(O)_2NH_2$,
- (c) $S(O)_2NHC(O)CF_3$,
- (d) $S(O)(NH)CH_3$,
 - (e) $S(O)(NH)NH_2$,
 - (f) $S(O)(NH)NHC(O)CF_3$,
 - (g) $P(O)(CH_3)OH$, and
 - (h) $P(O)(CH_3)NH_2$:

R² and R³ each are independently selected from the group consisting of:

- (a) hydrogen,
- (b) halo,
- (c) C₁-6alkoxy,
- C₁₋₆alkylthio, (d)
 - (e) CN,

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- (f) CF₃,
- (g). C₁₋₆alkyl, and
- (h) N3;
- R4 is selected from the group consisting of 10
 - hydrogen. (a)
 - (b) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET1, each of said phenyl, naphthyl or HET1 being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C1-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁶;
 - (c) phenyl, naphthyl or HET2, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁶;

R⁵ is selected from the group consisting of:

- -NOs, (a)
- (b) -C(O)-E-C₁₋₁₀alkyl-W-NO_s,
- (c)

$$\begin{array}{c} O & (R^{a})_{0-3} \\ -C - E - C_{0-6} alkyl - Ar - C_{0-6} alkyl - W - NO_{s}, \end{array}$$

wherein:

each s is independently 1 or 2,

E is a bond, oxygen, sulfur or -C(O)-O-,

each W is independently selected from the group consisting of:

30 **(1)** oxygen, sulfur,

(2)

(3)

$$\begin{array}{c} CO_{2}R^{b} \\ -C \\ -C \\ CO_{2}R^{b} \\ \end{array}$$
(4)
$$\begin{array}{c} O \quad CO_{2}R^{b} \\ -C -C \\ -C \\ R^{b} \end{array}$$

Ar is selected from the group consisting of: phenyl, naphthyl and HET3,

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each Ra is independently selected from the group consisting of:

- (1) halo,
- (2) C₁₋₆alkyl,
- (3) C₁₋₆alkoxy,
- (4) C₁₋₆alkylthio,
- (5) OH,
- (6) CN,
- (7) CF3,
- (8) CO_2R^7 , and

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(9) C_{0-6} alkyl-W-NO_s;

each Rb is independently selected from the group consisting of:

(1) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET⁴, each of said phenyl, naphthyl or HET⁴ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁸; and

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(2) phenyl, naphthyl or HET⁵, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁸;

 R^6 , R^7 and R^8 are each independently selected from the group consisting of

- (a) hydrogen,
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- (b) C₁₋₆alkyl; and

HET1, HET2, HET3, HET4 and HET5 are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, 5 indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, 10 dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisoxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, 15 dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

3. The compound according to Claim 2 wherein

 R^1 is $S(O)_2CH_3$, and

R² and R³ are both hydrogen.

4. The compound according to Claim 3 wherein:

R⁴ is C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET¹, each of said phenyl, naphthyl or HET¹ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and

30 CO_2R6 ;

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R6 is selected from the group consisting of

- (a) hydrogen,
- (b) C₁₋₆alkyl; and

HET1 is selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, 5 isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, 10 dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, 15 dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

- 5. The compound according to Claim 4 wherein R⁴ is methyl, ethyl, propyl or isopropyl.
 - 6. The compound according to Claim 3 wherein:
- R⁴ is phenyl, naphthyl or HET², each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁶;

R⁶ is selected from the group consisting of

- (a) hydrogen,
- 30 (b) C₁₋₆alkyl; and

HET² is selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carballyl, carballyl, indolnyl, indolnyl,

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isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, 5 piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, 10 dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

- The compound according to Claim 3 wherein R⁵ is -NO_S, 7.
- 15 wherein s is 1 or 2.
 - 8. The compound according to Claim 3 wherein R⁵ is -C(O)-E-C1-10alkyl-W-NOs, wherein:
- 20 s is 1 or 2,

E is a bond, oxygen, sulfur or -C(O)-O-, W is selected from the group consisting of:

- (1) oxygen,
- **(2)** sulfur,
- (3)

$$CO_2R^b$$
 $-C$
 CO_2R^b

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each Rb is independently selected from the group consisting of:

(1) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET⁴, each of said phenyl, naphthyl or HET⁴ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁸; and

phenyl, naphthyl or HET⁵, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁸;

R8 is selected from the group consisting of

- (a) hydrogen and
- (b) C₁₋₆alkyl; and

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HET⁴ and HET⁵ are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl,

- dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl,
 dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.
 - 9. The compound according to Claim 8 wherein:

E is a bond or oxygen:

s is 2;

W is oxygen; and

- 5 R4 is hydrogen, methyl, ethyl, propyl or isopropyl.
 - 10. The compound according to Claim 3 wherein R⁵ is

$$\begin{array}{c} O \\ -\overset{||}{C} - E - C_{0-6} alkyl - & C_{0-6} alkyl - W - NO_s \end{array}$$

wherein:

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each s independently 1 or 2,

15 E is a bond, oxygen, sulfur or -C(O)-O-,

each W is independently selected from the group consisting of:

- (1) oxygen,
- (2) sulfur,
- 20 (3)

$$CO_2R^b$$
 $-C$
 CO_2R^b

(4)
$$\begin{array}{ccc} O & CO_2R^b \\ -C - C & \\ R^b \end{array}$$

each Ra is independently selected from the group consisting of:

- 25 (1) halo,
 - (2) C₁₋₆alkyl,
 - (3) C₁₋₆alkoxy,
 - (4) C₁₋₆alkylthio,

- (5) OH,
- (6) CN,
- (7) CF₃,

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- (8) CO_2R^7 , and
- 5 (9) C_{0-6} alkyl-W- NO_{s} ;

each Rb is independently selected from the group consisting of:

- (1) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET⁴, each of said phenyl, naphthyl or HET⁴ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁸; and
- phenyl, naphthyl or HET⁵, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁸;

R7 and R8 is selected from the group consisting of

- (a) hydrogen and
- 20 (b) C₁₋₆alkyl; and

HET⁴ and HET⁵ are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroimidazolyl, dihydrooxadiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydro

dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

11. A compound according to Claim 2 of Formula II

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or a pharmaceutically acceptable salt thereof, wherein

R4 is selected from the group consisting of:

- (a) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET¹, each of said phenyl, naphthyl or HET¹ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁶;
- phenyl, naphthyl or HET², each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁶;

R⁶ is selected from the group consisting of

- (a) hydrogen and
- (b) C₁₋₆alkyl;

s is 1 or 2; and

HET¹ and HET² are each independently selected from the group consisting of: 30 benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl,

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benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxadiazolyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothianyl, dihydrotriazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothianyl, and tetrahydrothienyl.

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- 12. The compound according to Claim 11 wherein R⁴ is methyl, ethyl, propyl or isopropyl.
 - 13. The compound according to Claim 11 wherein

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 R^4 is phenyl or benzyl, wherein said phenyl and the phenyl portion of said benzyl are each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkylthio, OH, CN, CF3, and CO_2R^6 ; and

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R6 is selected from the group consisting of

- (a) hydrogen and
- (b) C₁₋₆alkyl.

- 14. The compound according to Claim 11 wherein s is 2.
- 15. A compound according to Claim 2 of Formula III

$$\begin{array}{c|c} CH_3SO_2 & W-NO_s \\ \hline \\ C_{0-6}alkyl \\ \hline \\ O \end{array}$$

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5 or a pharmaceutically acceptable salt thereof, wherein

R⁴ is selected from the group consisting of:

- (a) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET¹, each of said phenyl, naphthyl or HET¹ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁶;
- (b) phenyl, naphthyl or HET², each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C1-6alkyl, C1-6alkoxy, C1-6alkylthio, OH, CN, CF3, and CO₂R⁶;

R⁶ is selected from the group consisting of

- (a) hydrogen,
- (b) C₁₋₆alkyl;

20 Ra is hydrogen or Co-6alkyl-W-NOs.

each s is independently 1 or 2,

each W is independently selected from the group consisting of:

25 (1) oxygen,

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- (2) sulfur,
- (3)

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- 5 each Rb is independently selected from the group consisting of:
 - (1) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET⁴, each of said phenyl, naphthyl or HET⁴ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁸; and
 - phenyl, naphthyl or HET⁵, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁸;
- 15 R8 is selected from the group consisting of
 - (a) hydrogen,
 - (b) C₁₋₆alkyl; and

HET¹, HET², HET⁴ and HET⁵ are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydroimidazolyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroixadiazolyl, dihydroixadiazolyl, dihydrooxadiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyridinyl,

dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

- 5 16. The compound according to Claim 15 wherein R⁴ is methyl, ethyl, propyl or isopropyl.
 - 17. The compound according to Claim 15 wherein
- 10 R⁴ is phenyl or benzyl, wherein said phenyl and the phenyl portion of said benzyl are each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁶; and
- 15 R6 is selected from the group consisting of
 - (a) hydrogen and
 - (b) C₁₋₆alkyl.
- 18. The compound according to Claim 15 wherein s is 2 and W is 20 oxygen.
 - 19. The compound according to Claim 15 wherein R^a is -CH₂-W-NO_s.
- 25 20. A compound according to Claim 2 of Formula IV

$$CH_3SO_2 \xrightarrow{O} O \xrightarrow{V} C_{0-6}alkyl$$

$$CH_3SO_2 \xrightarrow{IV} O \xrightarrow{IV} R^a$$

5 or a pharmaceutically acceptable salt thereof, wherein

R4 is selected from the group consisting of:

- (a) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET¹, each of said phenyl, naphthyl or HET¹ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁶;
- (b) phenyl, naphthyl or HET², each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁶;

R6 is selected from the group consisting of

- (a) hydrogen,
- (b) C₁₋₆alkyl;
- 20 Ra is hydrogen or Co-6alkyl-W-NOs.

each s is independently 1 or 2;

each W is independently selected from the group consisting of:

25 (1) oxygen,

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(2) sulfur,

$$\begin{array}{c} CO_2R^b \\ -C \\ CO_2R^b \end{array}$$

$$\begin{array}{c}
-C - \\
CO_2 R^b, \\
O CO_2 R^b \\
-C - C - \\
R^b
\end{array}$$

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each Rb is independently selected from the group consisting of:

- (1) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET⁴, each of said phenyl, naphthyl or HET⁴ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁸; and
- phenyl, naphthyl or HET⁵, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁸;

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R8 is selected from the group consisting of

- (a) hydrogen,
- (b) C₁₋₆alkyl; and

HET¹, HET², HET⁴ and HET⁵ are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolazinyl, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydroimidazolyl, dihydroimidazolyl, dihydroimidazolyl, dihydroimidazolyl, dihydroimidazolyl, dihydroixadiazolyl, dihydroix

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dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidinyl, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl.

21. The compound according to Claim 20 of Formula IVa

or a pharmaceutically acceptable salt thereof, wherein

R⁴ is selected from the group consisting of:

- (a) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET¹, each of said phenyl,
 - naphthyl or HET¹ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁶;

C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁶;

(b) phenyl, naphthyl or HET², each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo,

R6 is selected from the group consisting of

- (a) hydrogen,
- 25 (b) C₁₋₆alkyl;

Ra is hydrogen or Co-6alkyl-W-NOs.

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each s is independently 1 or 2;

each W is independently selected from the group consisting of:

- (1) oxygen,
- (2) sulfur,

(3)
$$CO_2R^b$$
 $-C$ CO_2R^b

(4)

$$O CO_2R^b$$

 $-C-C-C-C$
 R^b

each Rb is independently selected from the group consisting of:

- (1) C₁₋₆alkyl, optionally substituted with 1-3 halo groups or optionally substituted with phenyl, naphthyl or HET⁴, each of said phenyl, naphthyl or HET⁴ being optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁₋₆alkyl, C₁₋₆alkoxy, C₁₋₆alkylthio, OH, CN, CF₃, and CO₂R⁸; and
- phenyl, naphthyl or HET⁵, each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁸;

R⁸ is selected from the group consisting of

- (a) hydrogen,
- (b) C₁₋₆alkyl; and

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HET¹, HET², HET⁴ and HET⁵ are each independently selected from the group consisting of: benzimidazolyl, benzofuranyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolyl, indolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthyridinyl, oxadiazolyl, oxazolyl, pyrazinyl, pyrazolyl,

pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidinyl, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothianyl, dihydrothiazolyl, dihydrothianyl, and tetrahydrothienyl, dihydrothienyl, and tetrahydrothienyl.

- 22. The compound according to Claim 21 wherein R⁴ is methyl, ethyl, propyl or isopropyl.
 - 23. The compound according to Claim 21 wherein

R⁴ is phenyl or benzyl, wherein said phenyl and the phenyl portion of said benzyl are each optionally substituted with 1-3 substituents independently selected from the group consisting of: halo, C₁-6alkyl, C₁-6alkoxy, C₁-6alkylthio, OH, CN, CF₃, and CO₂R⁶; and

R6 is selected from the group consisting of

- (a) hydrogen and
- (b) C₁₋₆alkyl.

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- 24. The compound according to Claim 21 wherein s is 2 and W is oxygen.
- 30 25. The compound according to Claim 21 wherein R^a is -CH₂-W-NO_S.
 - . 26. The compound according to Claim 1 wherein: R⁴ is C₁₋₆alkyl, mono-substituted with

(i) N(Rⁱ)Rⁱⁱ, wherein Rⁱ and Rⁱⁱ are each independently selected from the group consisting of hydrogen and C₁₋₄alkyl or

(ii) -CO₂Rⁱⁱⁱ, wherein Rⁱⁱⁱ is hydrogen or C₁-4alkyl.

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27. A compound selected from the following group:

or a pharmaceutically acceptable

salt thereof,

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or a pharmaceutically acceptable salt

10 thereof,

or a pharmaceutically acceptable salt

thereof,

or a pharmaceutically acceptable salt

thereof,

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or a pharmaceutically acceptable

salt thereof, and

28. A method of treating an inflammatory disease susceptible to treatment with a non-steroidal anti-inflammatory agent comprising administering to a patient in need of such treatment of a non-toxic therapeutically effective amount of a compound according to Claim 1.

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- 29. The method according to Claim 28 wherein the patient is also at risk of a thrombotic cardiovascular event.
- 30. A method of treating cyclooxygenase mediated diseases
 advantageously treated by an active agent that selectively inhibits COX-2 in
 preference to COX-1 comprising administering to a patient in need of such treatment
 of a non-toxic therapeutically effective amount of a compound according to Claim 1.
- 31. The method according to Claim 30 wherein the patient is also at risk of a thrombotic cardiovascular event.
 - 32. A method for treating a chronic cyclooxygenase-2 mediated disease or condition and reducing the risk of a thrombotic cardiovascular event in a human patient in need of such treatment and at risk of a thrombotic cardiovascular event comprising orally concomitantly or sequentially administering to said patient a compound according to Claim 1 in an amount effective to treat the cyclooxygenase-2 mediated disease or condition and aspirin in an amount effective to reduce the risk of the thrombotic cardiovascular event.
- 25 33. The method according to Claim 32 wherein the compound is administered orally on a once daily basis.
 - 34. The method according to Claim 32 wherein the compound is administered orally on a twice daily basis.

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35. The method according to Claim 32 wherein the cyclooxygenase-2 selective mediated disease or condition is selected from the group consisting of: osteoarthritis, rheumatoid arthritis and chronic pain.

36. The method according to Claim 32 wherein aspirin is administered at a dose of about 30 mg to about 1 g.

37. The method according to Claim 36 wherein aspirin is administered at a dose of about 80 to about 650 mg.

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- 38. The method according to Claim 37 wherein aspirin is administered at a dose of about 81 mg or about 325 mg.
- 39. The method according to Claim 32 wherein aspirin is orally administered once daily.
- 40. A pharmaceutical composition comprising a compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, and aspirin in combination with a pharmaceutically acceptable carrier.
 - 41. A pharmaceutical composition comprising a compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
 - 42. A compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, for use in medical therapy.
 - 43. A compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, for use in treating an inflammatory disease susceptible to treatment with a non-steroidal anti-inflammatory agent.
 - 44. Use of a compound of formula I according to any one of claims 1 to 27, or a pharmaceutically acceptable salt thereof, for use in the manufacture of a medicament for treating cyclooxygenase mediated diseases advantageously treated by selective inhibition of COX-2 in preference to COX-1